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(FILE 'HOME' ENTERED AT 13:31:39 ON 02 JUL 2003)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 13:31:55 ON 02 JUL 2003

```
L1          1085 S ENDOTHEL? (L) (SINGLE CELL)
L2           112 S L1 AND (EYE OR BRAIN OR CEREBRA? OR RETIA?)
L3            59 DUP REM L2 (53 DUPLICATES REMOVED)
L4            59 FOCUS L3 1-
L5             7 S L3 AND SUSPEN?
L6             7 SORT L5 PY
                 E QUINONERO JEROME?/AU
L7             5 S E2
L8            30 S E1
L9             0 S E7 AND E8
L10          106 S E7 OR E8
L11           35 S L7 OR L8
L12           22 DUP REM L11 (13 DUPLICATES REMOVED)
L13           22 SORT L12 PY
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FILE 'STNGUIDE' ENTERED AT 13:52:29 ON 02 JUL 2003

=> d an ti so au ab pi l13 14 16 18 20 21
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, SCISEARCH, CAPLUS' - CONTINUE? (Y)/N:y

L13 ANSWER 14 OF 22 SCISEARCH COPYRIGHT 2003 THOMSON ISI
AN 95:652122 SCISEARCH
TI AN IMMORTALIZED BRAIN ENDOTHELIAL-CELL LINE AS A VECTOR FOR GENE-THERAPY OF NEUROLOGICAL DISORDERS
SO JOURNAL OF CELLULAR BIOCHEMISTRY, (10 MAR 1995) Supp. 21A, pp. 390. ISSN: 0730-2312.
AU COURAUD P O (Reprint); **QUINONERO J**; TCHELINGERIAN J L; VIGNAIS L; JACQUE C; STROSBERG A D

L13 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2003 ACS
AN 1996:382921 CAPLUS
DN 125:50738
TI Immortalized lines of brain endothelial cells and therapeutic applications thereof
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
IN Chaverot, Nathalie; Couraud, Pierre-Olivier; Laterra, John; **Quinonero, Jerome**; Roux, Francoise; Strosberg, Arthur Donny; Tchelingerian, Jean-Leon; Vignais, Lionel
AB The invention relates to optionally modified immortalized lines of brain endothelial cells of mammals, as well as applications as preventive or curative drugs and particularly for the treatment of primary and secondary neurol. or psychiatric diseases, including brain tumors, and for stimulating the growth and reprodn. of breeding animals. The invention also relates to the method for prepg. said cell lines. The endothelial cell lines of mammalians disclosed are comprised of immortalized brain endothelial cells presenting at least one of the following characteristics of differentiated endothelial brain cells, in a stable way: the expression of endothelial markers, the secretion of vasoactive substances, the expression of mols. of the major histocompatibility complex (MHC), the expression of hormonal receptors, and the existence of tight junctions. Said cell lines comprise a nucleic acid fragment having at least one immortalizing fragment of a viral or cellular oncogene, optionally assocd. with at least one selection gene, and an expression vector comprising a sequence coding for a polypeptide, a protein or a viral vector, optionally assocd. with at least one selection gene and optionally at least one marker gene. The cell lines are capable of integrating into brain vessels of a host mammal and producing said polypeptide, protein or viral vector. Rat bran endothelial cells were immortalized by transfection with plasmid pE1A-neo, encoding the adenovirus E1A gene. Cell line RBE/NGF, expressing mouse .beta.-nerve growth factor (.beta.-NGF), was prepd. using retroviral vector pMoMuLVisisNGF. These cells were implanted into rat brains. The

grafts were not rejected, produced .beta.-NGF, and induced a biol. effect.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9611278	A1	19960418	WO 1995-FR1313	19951009
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2726005	A1	19960426	FR 1994-12078	19941010
	FR 2726005	B1	19970103		
	CA 2202066	AA	19960418	CA 1995-2202066	19951009
	AU 9536575	A1	19960502	AU 1995-36575	19951009
	AU 715289	B2	20000120		
	EP 787197	A1	19970806	EP 1995-934188	19951009
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10507074	T2	19980714	JP 1996-512390	19951009

L13 ANSWER 18 OF 22 MEDLINE
AN 97226860 MEDLINE
TI Gene transfer to the central nervous system by transplantation of cerebral endothelial cells.
SO GENE THERAPY, (1997 Feb) 4 (2) 111-9.
Journal code: 9421525. ISSN: 0969-7128.
AU **Quinonero J**; Tchelingerian J L; Vignais L; Foignant-Chaverot N; Colin C; Horellou P; Liblau R; Barbin G; Strosberg A D; Jacque C; Couraud P O
AB A cerebral endothelial immortalized cell line was used in transplantation experiments to deliver gene products to the adult rat brain. Survival of grafted cells was observed for at least 1 year, without any sign of tumor formation. When genetically modified to express bacterial beta-galactosidase and transplanted into the striatum, these cells were shown, by light and electron microscope analysis, to integrate into the host brain parenchyma and microvasculature. Following implantation into the striatum and nucleus basalis of adult rats, endothelial cells engineered to secrete mouse beta-nerve growth factor (NGF) induced the formation of a dense network of low-affinity NGF receptor-expressing fibers near the implantation sites. This biological response was observed from 3 to 8 weeks after engraftment. The present study establishes the cerebral endothelial cell as an efficient vector for gene transfer to the central nervous system.

L13 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2003 ACS
AN 2000:441660 CAPLUS
DN 133:53709
TI Pharmaceutical compositions comprising immortalized endothelial cells for use in the diagnosis and treatment of sources of angiogenesis
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
IN Timsit, Serge; **Quinonero, Jerome**
AB The invention discloses a pharmaceutical compn. to be used for diagnosing and/or treating angiogenic sources by being administered to a subject by systemic administration, the compn. contg.immortalized mammalian endothelial cells, optionally having an active substance for diagnosing and/or treating angiogenic sources.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000037112	A1	20000629	WO 1999-FR2965	19991130
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	FR 2787464	A1	20000623	FR 1998-16145	19981221
	FR 2787464	B1	20030110		

CA 2355879	AA	20000629	CA 1999-2355879	19991130	
EP 1140208	A1	20011010	EP 1999-973474	19991130	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002532567	T2	20021002	JP 2000-589222	19991130	

L13 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2003 ACS
AN 2000:441659 CAPLUS
DN 133:63922
TI Single cell-suspensions of transgenic animal cells for use in gene therapy without a risk of blocking minor vessels
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
IN Timsit, Serge; **Quinonero, Jerome**
AB Suspensions of mammalian cells transformed with a therapeutic gene with the cells forming very few or no aggregates are described for use in gene therapy by systemic administration. The invention is characterized in that it does not comprise aggregate of said cells having a size likely to cause temporary or permanent dysfunction in the subject. The invention also concerns pharmaceutical compns. comprising said prepn. and an acceptable carrier. Cultured transgenic cells were suspended by trypsinization and mixed by vigorous pipeting with a diluent before filtration through a 30 .mu. pore size filter. The final suspension had a cell d. of 1,000-300,000 per .mu.L. Rats infused with such cells were studied for the effects of the infusion. Of 48 rats, 4 died of respiratory or neurol. complications and one died of unknown causes. The remaining animals showed no ill effects and the infused cells became rapidly distributed throughout the brain.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000037111	A1	20000629	WO 1999-FR2964	19991130
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2787463	A1	20000623	FR 1998-16144	19981221
FR 2787463	B1	20010330		
CA 2355882	AA	20000629	CA 1999-2355882	19991130
EP 1140207	A1	20011010	EP 1999-973473	19991130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002532117	T2	20021002	JP 2000-589221	19991130

L4 ANSWER 2 OF 59 CAPLUS COPYRIGHT 2003 ACS
AN 1998:709171 CAPLUS
DN 129:313121
TI Use of nerve growth factor for the storage, culture or treatment of cornea
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
IN Lambiase, Alessandro
AB The nerve growth factor (NGF) is used for the storage of corneas in culture, for the prodn. and the storage in vitro of **single cell** populations of the corneal morphol. and functional unit (i.e., epithelium, stroma/keratocytes and **endothelium**) and of the conjunctival epithelium, and for the prodn. and the storage of corneal and conjunctival tissues, in particular for transplantation purposes. In an evaluation of the effects of NGF addn. to various culture media for explanted corneas (both at 5.degree. and at 30-36.degree.), the optimal response was obtained with a concn. of .apprx.100 ng/mL. Specifically, after 7 days of culture the improvements obtained were an increase of **endothelial** cell d. (from 10 to 25%), a redn. of **endothelial** cell mortality (absence of trypan blue-pos. cells), a better epithelial morphol., a higher viability of keratinocytes, and a markedly better appearance of the epithelium. In addn., some corneas that before being placed in culture were considered not suitable for transplantation turned out to be suitable after being cultured for 7 days in presence of NGF. Conjunctival epithelial cell cultures also show a proliferation and differentiation increase, as well an an increase in the no. of goblet cells, when cultured in the presence of murine NGF. The administration is NGF in **endothelial** pathologies, both of a dystrophic nature and acquired, both with loss of the no. of **endothelial** cells and with loss of the functionality thereof, restores a proper **endothelial** function. The NGF is also proposed for use in the therapy and/or the prophylaxis of diseases of the corneal surface, wherein a lack of integrity of the corneal and conjunctival morphol. and functional unit occurs, in particular for pathologies having a dystrophic or neurodystrophic basis, both congenital and acquired.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9848002	A1	19981029	WO 1997-IT292	19971121
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9851350	A1	19981113	AU 1998-51350	19971121
AU 513506	B2	20010621		
EP 973872	A1	20000126	EP 1997-946052	19971121
EP 973872	B1	20010711		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 203054	E	20010715	AT 1997-946052	19971121
ES 2162331	T3	20011216	ES 1997-946052	19971121
JP 2002507190	T2	20020305	JP 1998-545385	19971121
US 2002037584	A1	20020328	US 1999-403568	19991025
US 6537808	B2	20030325		
US 2003096413	A1	20030522	US 2003-337853	20030108

(FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 15:09:06 ON 02 JUL 2003)

DEL HIS

L1 230 S RBE4 (L) ENDOTHE?
L2 94 DUP REM L1 (136 DUPLICATES REMOVED)
L3 18 S L1 AND (AGGRE? OR SINGLE? OR MICRON?)
L4 18 FOCUS L3 1-
L5 61 S L1 AND (TRANSFECT OR TRANSFORMED OR GENE)
L6 8 S L5 AND (GROWTH FACTOR)
L7 5 DUP REM L6 (3 DUPLICATES REMOVED)

=> d an ti so au ab l7 5

L7 ANSWER 5 OF 5 MEDLINE DUPLICATE 2
AN 94186550 MEDLINE
TI Regulation of gamma-glutamyl transpeptidase and alkaline phosphatase activities in immortalized rat brain microvessel endothelial cells.
SO JOURNAL OF CELLULAR PHYSIOLOGY, (1994 Apr) 159 (1) 101-13.
Journal code: 0050222. ISSN: 0021-9541.
AU Roux F; Durieu-Trautmann O; Chaverot N; Claire M; Mailly P; Bourre J M; Strosberg A D; Couraud P O
AB Rat brain microvessel **endothelial** cells were immortalized by transfection with a plasmid containing the E1A adenovirus **gene**. One clone, called **RBE4**, was further characterized. These cells display a nontransformed phenotype and express typical **endothelial** markers, Factor VIII-related antigen and Bandeiraea simplicifolia binding sites. When **RBE4** cells were grown in the presence of bFGF and on collagen-coated dishes, confluent cultures developed sprouts that extend above the monolayer and organized into three-dimensional structures. The activity of the blood-brain barrier-associated enzyme, gamma-glutamyl transpeptidase (gamma GTP), was expressed in these structures, not in the surrounding monolayer. Similar results were obtained with the microvessel-related enzyme alkaline phosphatase (ALP). Addition of agents that elevate intracellular cAMP reduced the formation of three-dimensional structures, but every cell inside the aggregates still expressed gamma GTP and ALP activities. Such structures, associated with high levels of gamma GTP and ALP activities, were also induced by astroglial factors, including (1) plasma membranes from newborn rat primary astrocytes or rat glioma C6 cells, (2) C6 conditioned media, or (3) diffusible factors produced by primary astrocytes grown in the presence of, but not in contact with **RBE4** cells. **RBE4** cells thus remain sensitive to angiogenic and astroglial factors for the expression of the blood-brain barrier-related gamma GTP activity, as well as for ALP activity, and could constitute the basis of a valuable in vitro model of the blood-brain barrier.

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L4 ANSWER 6 OF 59 MEDLINE
AN 97053148 MEDLINE
TI Cultured vascular endothelial cells of the **brain**.
SO KEIO JOURNAL OF MEDICINE, (1996 Sep) 45 (3) 183-98; discussion 198-9.
Ref: 212
Journal code: 0376354. ISSN: 0022-9717.
AU Deli M A; Joo F
AB The **endothelium** is a **single-cell** lining the blood vessels and represents an interface between blood and tissue. It acts as a selective permeability barrier, regulates coagulation and contributes to the behaviour of cells both in the circulation and in the vessel wall. Because of its location, one of the most important function of the **endothelium** is the regulation of the movement from the vascular to the extravascular space of water and solutes containing nutrients. Recent advances in our knowledge of the blood-**brain** barrier (BBB) have in part been made by studying the properties and function of **cerebral endothelial** cells (CECs) in vitro. After an era working with a fraction, enriched in **cerebral** microvessels by centrifugation, the next generation of in vitro BBB model systems was introduced, when the conditions for routinely culturing the **endothelial** cells were established. This review summarizes the results from this rapidly growing field. In addition to providing a better insight into the chemical composition of CECs, much has been learned from these studies about the characteristics of transport processes and cell-to-cell interactions during the last years. Astrocytes and neuronal elements contribute to the induction of BBB properties of CECs during ontogenesis and in tissue culture conditions. With the application of new technologies, the approach offers new means to investigation, applicable not only to biochemistry and physiology but also to the drug research, and may improve the transport of substances through the BBB. CECs grown on microporous cell culture inserts and co-cultured with astrocytes or treated by astrocyte-conditioned media proved to be excellent models for studying the direct effects of mediators and second messengers on the transendothelial permeability. The in vitro approach has been and should remain an excellent model of the BBB to help unravel the complex molecular interactions underlying and regulating the permeability of **cerebral endothelium**.

L Number	Hits	Search Text	DB	Time stamp
1	3	WO NEAR "9306222"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/02 12:18
7	5	WO ADJ "8905345"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/02 12:29
31	1954	endothe$5 SAME (supension or non-aggregat$5 or aggregat$5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/02 13:08
37	587	(endothe$5 SAME (supension or non-aggregat$5 or aggregat$5)) AND (cerebra$5 retina$5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/02 13:02
43	55	((endothe$5 SAME (supension or non-aggregat$5 or aggregat$5)) AND (cerebra$5 retina$5)) and immortal$5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/02 13:08
49	2071	endothe$5 SAME genetic$5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/02 13:08
55	527	(endothe$5 SAME genetic$5) and immortal$5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/02 13:08
67	430	((endothe$5 SAME genetic$5) and immortal$5) and (brain or cerebra$5 or retina$5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/02 13:12
85	4	QUINONERO NEAR Jerome	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/02 13:13
91	9	(US-6001350-$ or US-5460959-$).did. or (WO-9306222-$ or WO-8905345-$ or WO-37112-$ or WO-37111-$ or FR-2787463-$).did. or (WO-9611278-$ or EP-391960-$).did.	USPAT; EPO; DERWENT	2003/07/02 13:28

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A61K 48/00, C12N 5/10, A61P 25/00	A1	WO 00/37111
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(22) Date de dépôt international: 30 novembre 1999 (30.11.99)

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(71) Déposant *(pour tous les Etats désignés sauf US)*: NEUROTECH (S.A.) [FR/FR]; Parc Club Orsay, 2, rue Jean Rostand, Bâtiment D, F–91893 Orsay (FR).

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(75) Inventeurs/Déposants *(US seulement)*: TIMSIT, Serge [FR/FR]; 112 Ter, avenue de Suffren, F–75015 Paris (FR). QUINONERO, Jérôme [FR/FR]; 5, cours du Luzard, F–77186 Noisiel (FR).

(74) Mandataires: BREESE, Pierre etc.; Breese–Majerowicz, 3, avenue de l'Opéra, F–75001 Paris (FR).

(81) Etats désignés: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, brevet ARIPO (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), brevet eurasien (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), brevet européen (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), brevet OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Publiée
Avec rapport de recherche internationale.

(54) Title: MAMMALIAN CELL PREPARATIONS OPTIONALLY TRANSFECTED WITH A GENE CODING FOR AN ACTIVE SUBSTANCE CONTAINING SAME

(54) Titre: PREPARATIONS DE CELLULES DE MAMMIFERE EVENTUELLEMENT TRANSFECTEES AVEC UN GENE CODANT POUR UNE SUBSTANCE ACTIVE ET LES CONTENANT

(57) Abstract

The invention concerns a mammalian cell preparation optionally transfected with at least a gene coding for an active substance capable of being administered to a subject by systemic administration. The invention is characterised in that it does not comprise aggregate of said cells having a size likely to cause temporary or permanent dysfunction in the subject. The invention also concerns pharmaceutical compositions comprising said preparation and an acceptable carrier.

(57) Abrégé

La présente invention a pour objet une préparation de cellules de mammifère éventuellement transfectées avec au moins un gène codant pour une substance active, pour être administrée par voie sytémique chez un sujet, caractérisée en ce qu'elle ne comprend pas d'agrégat desdites cellules d'une taille susceptible d'entraîner chez ledit patient des dysfontionnements transitoires ou permanents. L'invention concerne aussi les compositions pharmaceutiques comprenant une telle préparation et un véhicule acceptable.

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Search	Most Recent Queries	Time	Result
#59	**Related Articles** for **PubMed** (Select **7909803**)	14:55:53	161
#57	Search **RBE4** Field: **All Fields,** Limits: **Publication Date to 1994**	14:52:43	4
#56	Search **RBE4** Field: **Author,** Limits: **Publication Date to 1994**	14:52:33	0
#55	**Related Articles** for **PubMed** (Select **7908023**)	14:52:00	197
#53	Search **Couraud PO** Field: **Author,** Limits: **Publication Date to 1994**	14:48:48	39
#51	Search **Ferry N** Field: **Author,** Limits: **Publication Date to 1994**	14:46:51	60
#50	Search **RBE4 OR RBEZ**	14:45:06	67
#49	Search **RBE4 RBEZ**	14:43:32	1
#47	Search **endothelial RBE4 RBEZ** Field: **All Fields**	14:41:10	1
#46	Search **endothelial RBE4 RBEZ** Field: **All Fields,** Limits: **Publication Date to 1994**	14:40:58	0
#45	Search **endothelial RBE4** Field: **Author,** Limits: **Publication Date to 1994**	14:40:46	0
#44	Search **Roux F** Field: **Author,** Limits: **Publication Date to 1994**	14:40:17	153
#43	Search **claire m** Field: **Author,** Limits: **Publication Date to 1996**	14:37:36	34
#41	Search **LAL B** Field: **Author,** Limits: **Publication Date from 1994 to 1994**	14:34:48	4
#39	**Related Articles** for **PubMed** (Select **9081701**)	14:34:24	185
#37	Search **Quinonero J** Field: **Author**	14:31:45	8

1: J Cell Physiol. 1994 Apr;159(1):101-13. Related Articles, Links

Regulation of gamma-glutamyl transpeptidase and alkaline phosphatase activities in immortalized rat brain microvessel endothelial cells.

Roux F, Durieu-Trautmann O, Chaverot N, Claire M, Mailly P, Bourre JM, Strosberg AD, Couraud PO.

INSERM U26, Hopital F. Widal, Paris, France.

Rat brain microvessel endothelial cells were immortalized by transfection with a plasmid containing the E1A adenovirus gene. One clone, called RBE4, was further characterized. These cells display a nontransformed phenotype and express typical endothelial markers, Factor VIII-related antigen and Bandeiraea simplicifolia binding sites. When RBE4 cells were grown in the presence of bFGF and on collagen-coated dishes, confluent cultures developed sprouts that extend above the monolayer and organized into three-dimensional structures. The activity of the blood-brain barrier-associated enzyme, gamma-glutamyl transpeptidase (gamma GTP), was expressed in these structures, not in the surrounding monolayer. Similar results were obtained with the microvessel-related enzyme alkaline phosphatase (ALP). Addition of agents that elevate intracellular cAMP reduced the formation of three-dimensional structures, but every cell inside the aggregates still expressed gamma GTP and ALP activities. Such structures, associated with high levels of gamma GTP and ALP activities, were also induced by astroglial factors, including (1) plasma membranes from newborn rat primary astrocytes or rat glioma C6 cells, (2) C6 conditioned media, or (3) diffusible factors produced by primary astrocytes grown in the presence of, but not in contact with RBE4 cells. RBE4 cells thus remain sensitive to angiogenic and astroglial factors for the expression of the blood-brain barrier-related gamma GTP activity, as well as for ALP activity, and could constitute the basis of a valuable in vitro model of the blood-brain barrier.

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